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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/225,426	01/05/99	ROSAZZA J	P00297US1

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EXAMINER	
SAUCIER,S	
ART UNIT	**PAPER NUMBER**
1651	10

DATE MAILED: 11/08/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/225,426	Rosazza t al.
Examiner	**Group Art Unit**
Sandra Saucier	1651

☒ Responsive to communication(s) filed on *Apr 25, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-15* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-15* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Claims 1-15 are pending and under examination.

Election/Restriction

Applicant has elected the species of "arginine rich peptides" in paper #9 for examination. The claims have been examined to the extent that they read on arginine rich peptides. Should no art be found for this elected class, the examiner will pick another class for further examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112: The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Dosages which are critical or essential to the practice of the invention, but not included in the claims is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The specification must teach how to use the claimed invention to regulate NO production in a mammalian subject. The specification does not fulfill this requirement because neither dosages of the various "drugs" or inhibitors, which belong to the classes of peptides, oligopeptides or proteins are given in the generic disclosure of the invention.

Nor are there examples of dosages of these agents given to any mammal which effects a measurable response which might be interpreted as NO production decrease or increase from which one of skill in the art might extrapolate to all mammals.

The only examples are of additions of certain peptides and oligopeptides to a purified NO synthase in a test tube. This is not an art accepted model, the results of which which may be readily extrapolated to an *in vivo* system. Further, no evidence is of record that such a system which can correlate this *in vitro* test-tube method with purified NO synthase to *in vivo* dosages of agents which inhibit or enhance NO syntase activity in an intact mammal exists in the prior art.

Instead, the specification states that "a therapeutically effective amount" of a peptide is an amount sufficient to effect a response to nNOS-II. This is merely a circular definition, and is not sufficient guidance to enable one of skill to practice the invention without undue experimentation; rather it is merely an invitation to experiment.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7 and 10 are indefinite because the intent of the claims is not clear. It is not clear if the modifier "arginine rich" is intended to modify oligopeptide and protein or only modify peptide. It is not clear if "inhibitor of NOS" is intended to modify only protein or if it is intended to also modify peptide and oligopeptide. Thus, the scope of the claims in uncertain.

Also, "arginine rich" is a term of comparison. Rich in comparison to what? No reference point has been supplied for this term and it is, thus, indefinite.

Claims 3, 4, 13 and 14 are rejected because they do not further limit the independent claims. The substances mentioned are not peptides, oligos or proteins.

Claim 6 is rejected because it is inconsistent with the independent claim. An inhibitor of NOS would not be expected to increase the production of NO.

Claims 7 and 8, it is unclear what is meant by "the nitric oxide syntase of claim 1 or 2". There is no nitric oxide syntase in the preambles of claim 1 or 2. The phrase at the end of claim 1 is "or protein inhibitor of nitric oxide syntase". This defines the protein, not the mechanism of regulating or controlling NO production.

Likewise, claim 11 is unclear. Are applicants attempting to claim the mechanism of action of the administration of the agents? Please note that no inhibition of NOS is required by the independent claim. The only mention of NOS is as a modifier for the protein agent.

Claim 12 is ambiguous and unclear. Claim 10 on which it depends is directed to the treatment of an (intact) mammalian subject, while claim 12 appears to be directed to the inhibition of a purified protein. The claim makes no sense and is completely uninterpretable.

To the extent that applicants' intend to argue that the dosages of peptides to be administered are known in the art, the following rejections have been applied.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 6, 10-12 and 15 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Norryd *et al.* [U].

The claims are directed to a one-step adminstration of a peptide to regulate NO production or to treat an NO-mediated disease.

Norryd *et al.* disclose the administration of bradykinin by injection into an artery. Bradykinin is a peptide of 9 amino acids which contains two arginines.

Although the reference is silent with regard to the claimed end result of inhibiting nNOS-II, this result is regarded as being inherent in the one-step method of administering bradykinin.

If applicant argues that the reference does not teach the penetration of bradykinin through the blood-brain barrier, and thus, the administered bradykinin cannot inhibit nNOS-II, a rejection directed to the enablement of the specification with regard to the blood-brain barrier problem may be applicable.

Please note that claims 3, 4, 13 and 14 are not directed to peptides; therefore, they have not been examined for prior art.

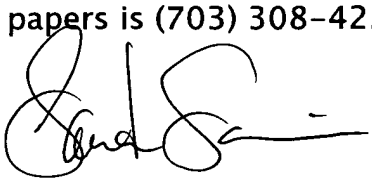
Claims 1, 2, 5-12, 15 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Groves *et al.* [V].

Groves *et al.* disclose the one-step method of the administration of regulators of NO production, bradykinin and HOE-140, a bradykinin B2 receptor antagonist to a human. This reference fulfills the one step method of administering a NO-regulating amount of an peptide. Bradykinin, an arginine containing peptide, stimulates the production of NO and vasodilation, while the peptide, HOE-140, which is a known bradykinin antagonist, constricts the coronary artery which is a measure of the production of NO.

In order to qualify as an anticipatory reference, the disclosure need not be express, but may anticipate by inherency. Failure of those skilled in the art to contemporaneously recognize an inherent propery, function or ingredient of a prior art reference does not preclude a finding of anticipation: In *Atlas Powder Co. v. IRECO, Inc.*, 51 USPQ2d 1943 (Fed. Cir. 1999).

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Service Desk at (703) 308-0196. The number of the Fax Center for the faxing of papers is (703) 308-4227.



Sandra Saucier
Primary Examiner
Art Unit 1651
October 26, 2000